Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREC Inventor(s): Daniel J. DRUCKE Appl. No.: 09/833,740

		FIG.	1a		
970 AGGTTTACCG TCCAAATGGC	980 CATTTTGACA GTAAAACTGT	990 CTAGATGGCA GATCTACCGT	1000 TCCGTCCCAC AGGCAGGGTG	1010 GGGTAGCAGG CCCATCGTCC 1070	1020 TCATGAAGCT AGTACTTCGA 1080
1030 GACCAAGGCA CTGGTTCCGT 1090	1040 AGTCCTTTCA TCAGGAAAGT 1100	1050 GGGGGAAGAA CCCCCTTCTT 1110	1060 AATCAGGAAA TTAGTCCTTT 1120	AAAAAAAATT TTTTTTTAA 1130	TTAGAAĞCAT AATCTTCGTA 1140
TTCAAGAAGC AAGTTCTTCG	AAGATGĞĀĀŤ TTCTACCTTA	ATTTGTĀČĀĀ TAAACATGTT 1170	AACAGGTĞĞT TTGTCCACGA 1180	TTCTCCCCCA AAGAGGGGGT 1190	CCATGCGACC GGTACGCTGG 1200
1150 CGGGAGCTCC GCCCTCGAGG	1160 ACTGATATGG TGACTATACC 1220	ACAGAATAGC TGTCTTATCG 1230	TTTACAGCTA AAATGTCGAT 1240	CATTCAÁÁAC GTAAGTTTTG 1250	ACACACÁCÁC TGTGTGTGTG 1260
ACACACACAC TGTGTGTGTG	ACACACĀCĀC TGTGTGTGTG	ACACACĀČĀČ TGTGTGTGTG	ACACACACAT TGTGTGTGTA 1300	GTTTTCTTCC CAAAAGAAGG 1310	CTCCCTCCĂC GAGGGACCTC 1320
1270 TTCCTCCCAT AAGGAGGGTA	1280 TCTCTGTGGT AGAGACACCA	1290 CCCAAAGAGA GGGTTTCTCT	TGACCATÁTT ACTGGTATAA	GACTGTÁGÁÁ CTGACATCTT 1370	ATCACACCAC TAGTGTGGTG 1380
1330 CATAAAAGCC GTATTTTCGG	1340 CATCTGGGAG GTAGACCCTC	1350 CCATTTCCAG GGTAAAGGTC	ACTGATCTTT TGACTAGAAA	TTATCATTAA AATAGTAATT	GGTTTGAATT CCAAACTTAA 1440
1390 CTTGCCACGT GAACGGTGCA	1400 GTGGGTTTTA CACCCAAAAT	1410 AGGTTTTTAG TCCAAAAATC	1420 GGATTTTAT CCTAAAAATA	1430 CTAGCGGCAC GATCGCCGTG	TCACCTGCTT AGTGGACGAA
1450 CCCTGTGAAT GGGACACTTA	1460 GTTCAGAATT CAAGTCTTAA	1470 CACTGGGCTT GTGACCCGAA	1480 GGTCAGCTAA CCAGTCGATT	1490 TGGAAATGAT ACCTTTACTA	CTATGGTTTG GATACCAAAC
1510 ACTTAAATGT TGAATTTACA	1520 GAAAGGAAAA CTTTCCTTTT	1530 AAAAGAAGGG TTTTCTTCCC	1540 GGAAAAGGAG CCTTTTCCTC	1550 GGAGGGAGAA CCTCCCTCTT	1560 AGAGGGGAAG TCTCCCCTTC
1570 GGAAAACTGC CCTTTTGACG	1580 CTTTTATGCC GAAAATACGG	1590 TATTGCTACT ATAACGATGA	1600 CTAACATTTT GATTGTAAAA	1610 GTCTCTCACC CAGAGAGTGG	1620 TTCCACTTGG AAGGTGAACC
1630 TTCTTCAATG AAGAAGTTAC	1640 GAAAGACTGG CTTTCTGACC	1650 ATAGAAAGCT TATCTTTCGA	1660 GGGAGCCAGC CCCTCGGTCG	1670 CAGGGATAGG GTCCCTATCC	1680 AGGAGTGTGT TCCTCACACA
1690 GTGTGTGTGG CACACACACC	1700 GGGGGGGTGG CCCCCCACC	1710 GCAGCAAGCA CGTCGTTCGT	1720 GAGCCTTAGA CTCGGAATCT	1730 GACAGAGAAG CTGTCTCTTC	1740 AGCCTGCTAG TCGGACGATC 1800
1750 AGAYCATGAG TCTRGTACTC	1760 CTTYCTTTGA GAARGAAACT	1770 GACCCCTAGT CTGGGGATCA	1780 GCTAACAGGA CGATTGTCCT	1790 ATAGTTCCTA TATCAAGGAT	ACCAGGTAGC TGGTCCATCG
1810 TGTGGTCACG ACACCAGTGC	1820 Tgactcggct Actgagccga	1830 GGAAGSCCTG CCTTCSGGAC	1840 GCTTTGTCTT CGAAACAGAA	1850 TTTGCTTGCT AAACGAACGA	1860 GTGCAGCCTT CACGTCGGAA

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREOF Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

FIG. 1b

		rig.	ID	•	1 1 2 th 2 th 3
1870 GAACAAACAC CTTGTTTGTG	1880 CCTGGCCTCT GGACCGGAGA	1890 TTGAACCCCA AACTTGGGGT	1900 CTATTTCTCA GATAAAGAGT 1960	1910 GCCCTCAGAT CGGGAGTCTA 1970	1920 GAAGAAGTAA CTTCTTCATT 1980
1930 TGGTACCTTG ACCATGGAAC	1940 GAGGATACTG CTCCTATGAC	1950 ATGGGTTCAA TACCCAAGTT	GTGAACTAGG CACTTGATCC 2020	GCAGAGGGTG CGTCTCCCAC 2030	GAAGGTTTTG CTTCCAAAAC 2040
1990 TAACCATAAA ATTGGTATTT	2000 CTGAAGTGGG GACTTCACCC	2010 GTGTTGGTTA CACAACCAAT	GTAAGTAGCC CATTCATCGG 2080	ATGAATÁCCÁ TACTTATGGT 2090	TAAAAATÄTČ ATTTTTATAG 2100
2050 TGTCAGGTGG ACAGTCCACC	2060 CCAGAGCATC GGTCTCGTAG	2070 ACTGTGTTCA TGACACAAGT 2130	GAACACAACG CTTGTGTTGC 2140	GCCCACTCÁĞ CGGGTGAGTC 2150	AACACGĒĞĀ TTGTGCGCCT 2160
2110 CAATTGAAAG GTTAACTTTC	2120 GCACCAACCT CGTGGTTGGA	CCGTGCTTCC GGCACGAAGG 2190	TACCCGTTGT ATGGGCAACA 2200	TTTGTTÄČČĞ AAACAATGGC 2210	TGTAAAĈĠĈĀ ACATTTGCGT 2220
2170 ACTCAACTCT TGAGTTGAGA	2180 CGGCACTGAA GCCGTGACTT	CAGGCTTTTG GTCCGAAAAC 2250	CTGCAGACCT GACCTCTGGA 2260	GGGGTCTĞĞĂ CCCCAGACCT 2270	GGTGTTGTCT CCACAACAGA 2280
2230 CTGAGACAGG GACTCTGTCC	2240 AAAACTCATC TTTTGAGTAG 2300	TTGTTACTAT AACAATGATA 2310	GGCATAGTAG CCGTATCATC 2320	TAACCACGGĂ ATTGGTGCCT 2330	GCTCTGAGAT CCAGACTCTA 2340
2290 AGCCCTGAGC TCGGGACTCG	TGGTGCCGTT ACCACGGCAA	TAGAAAAGTT ATCTTTTCAA 2370	TGATGCTTTA ACTACGAAAT 2380	GAAAGAÄÄTČ CTTTCTTTAG 2390	GTGGCTTAAA CACCGAATTT 2400
2350 AGAAGCCTAC TCTTCCGATG	2360 CTGGCATGGG GACCCTACCC	GGCCCATCCT CCGGGTAGGA 2430	CTCCAGCCAT GAGGTCGGTA 2440	CCGAATČŤČÁ GGCTTAGAGT 2450	ATCTGGTCGT TAGACCAGCA 2460
2410 GTGCGTAAGA CACGCATTCT	2420 ATAGAATCCT TATCTTAGGA	CGGAATGGTA GCCTTACCAT 2490	ACCATGTCTT TGGTACAGAA 2500	GCTTTTTČŤŤ CGAAAAAGAA 2510	CTGGGCTTGC GACCCGAACG 2520
2470 TGAGGAAGTC ACTCCTTCAG	2480 CCAGGCAGCG GGTCCCTCGC	TAGACGTCTT ATCTGCAGAA 2550	GGGGGTAGGT CCCCCATCCA 2560	CTGGGAĀĀĀĀ GACCCTTTTT 2570	TCTCCCĀĀGĀ ĀGĀGGGTTCT 2580
2530 TTTTAGGAGG AAAATCCTCC	2540 GGCAGGCGGG CCGTCCGCCC unitive transcr	GGATGAGAAA	CTTGGAGATT GAACCTCTAA	CGGTAGATCG GCCATCTAGC	CTGTAGÄĞCÄ GACATCTCGT 5'- race product).
		2610	2620	2630	2640
2590 ACTCAGACAG TGAGTCTGTC	2600 TCGGCGGCCT AGCCGCCGGA	GAAGAGGACT CTTCTCCTGA	2620 TGTGCAAACA ACACGTTTGT	CTTCCTCTCT GAAGGAGAGA 2690	GGACAAĞĞAĞ CCTGTTCCTC 2700
2650 GAATGCAGGA CTTACGTCCT	2660 GGCCACCGCC CCGGTGGCGG	2670 TGCAGTACAT ACGTCATGTA	2680 CTTGGAGTGT GAACCTCACA	TGGAGGGATG ACCTCCCTAC	TGCCTGCACT ACGGACGTGA /human GLP-2R gene.
		esponds to tra	07.01 10 10 10 10 10 10 10	2750	2760
2710 TGTGAAAGGG ACACTTTCCC	2720 CGCCAGAAGG GCGGTCTTCC	ACGAGGCCCC TGCTCCGGGG	2740 AACCAAGCCC TTGGTTCGGG	GGCAGTGCCC CCGTCACGGG 2810	AGTAGATĞČÄ TCATCTACGT 2820
2770 GAGAGCGTCC CTCTCGCAGG	2780 CTGCCCCGGG GACGGGGCCC	2790 CGCACAGTWG GCGTGTCAWC	2800 GGCTCCCTGC CCGAGGGACG	GGCCCAGGGG CCGGGTCCCC	CCTGAGTČTČ GGACTCAGAG

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREOF Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

FIG. 1c

Putative translational start site in murine GLP-2 Receptor gene.

	1			2070	2880
2830 TCCACKCCCA AGGTGMGGGT	2840 CGGGATGCGT GCCCTACGCA	2850 CGGCTCTGGG GCCGAGACCC	2860 GCCCTGGGAC CGGGACCCTG	2870 GCCCTTCCTC CGGGAAGGAG	TCCCTGCTTC AGGGACGAAG
2890	2900	2910	2920	2930	2940
TGCTGGTTTC	CATCAAGCAA	GTAAGAACAG	ATTTTTATTC	CTCATTCGTC	TTGTTAATAT
ACGACCAAAG	GTAGTTCGTT	CATTCTTGTC	TAAAAATAAG	GAGTAAGCAG	AACAATTATA
2950	2960	2970	2980	2990	3000
TATCAGTTGT	GCATGTTTTC	TGAGTGTACA	AGCAATTTAG	GCCCCGTGTA	GGCAATTTGG
ATAGTCAACA	CGTACAAAAG	ACTCACATCT	TCGTTAAATC	CGGGGCACAT	CCGTTAAACC
3010	3020	3030	3040	3050	3060
GTAAGAATAA	AACCATATTA	AGAAAATGAG	GCTCAACCAC	AACCCCAGTA	GCATTCTGCT
CATTCTTATT	TTGGTATAAT	TCTTTTACTC	CGAGTTGGTG	TTGGGGTCAT	CGTAAGACGA
3070	3080	3090	3100	3110	3120
CACTGTTCAT	ATTTTGGCTG	ATTTTTAAAA	AAATTCTCTT	TTCTGTGCAT	TATTTTACAC
GTGACAAGTA	TAAAACCGAC	TAAAAATTTT	TTTAAGAGAA	AAGACACGTA	ATAAAATGTG
3130 AGCCGAAATT TCGGCTTTAA	3140	3150	3160	3170	3180

3'-End of murine GLP-2 Receptor gene sequenced to date.

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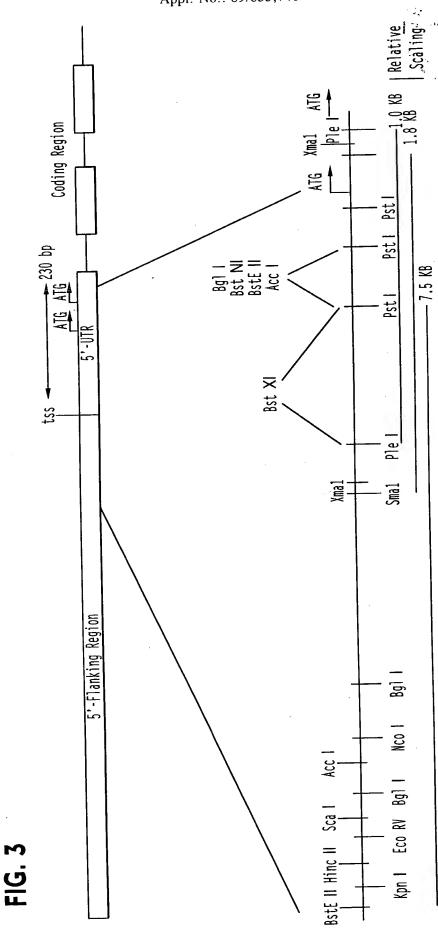
Com. my

FIG. 2 Sequence alignment of the 5' end of the mGLP-2 receptor gene with the 5' end of the cDNA encoding the rat GLP-2R.

Putative t	ranscripti •	ional start si	ite.	ŗ	5'-UTR nearly	identical
					petween rat and sequences encodend of GLP-2R.	ding 5'
		10	20	30	40	50
MOUSE GLP-2R RAT GLP-2R	1 1	AACACTTCĈT AACACTTCCT	CTCTGGACÃĂ CTCTGGACÃĂ	GGAGGAATGC GGAGGAGTGC	AGGAGGCCAC AGGAGGCCAC	CGCCTGCAGT CGCCTGCAGT
MOUSE GLP-2R RAT GLP-2R	51 51	60 ACATCTTGGA ACATCTTGGA	70 GTGTTGGAGG GTGTTGGAGG	80 GATGTGCCTG GATGTGCCTG	90 CACTTGTGAA CACTTGTGAA	AGGGCCCCAG CGGGCGCCAG
MOUSE GLP-2R RAT GLP-2R	101 101	110 AAGGACGAGG GAGAATGAGG	120 CCCCAACCAA CCCCAACCAA	130 GCCCGGCAGT GCCCGGCAGT	140 GCCCAGTAGA GCCCAGTAGA	150 TGCAGAGAGC TGCAGAGAGAG
MOUSE GLP-2R RAT GLP-2R	151 151	160 GTCCC-TGCC CACCCGTGCC	170 CCGGGC CCGAGTGAGG	180 GCACAG GCACAGCCAG	190 TWGGGCTCCC TGGGCATCCC	200 TGCGGCCCAG TGAGGCCCAG
MOUSE GLP-2R RAT GLP-2R	201 201	210 GGGC¢TGAGT GGGC¢CGTTC	220 CTCTCCACKC CTCTCCACTC	230 CCACGGGATG CCAACAG <u>ATG</u>	240 CGTCGGCTCT CGTCTGCTGT	250 GGGGCCCTGG GGGGCCCTGG
MOUSE GLP-2R RAT GLP-2R	251 251	260 GACGCCCTTC GAGGCCCTTC	270 CTCTCCCTGC CTCGCCCTGC	280 TTCTGCTGGT TTCTGCTGGT	290 TTCCATCAAG TTCCATCAAG	300 CAAGTAAGAA CAAGTTACAG
MOUSE GLP-2R RAT GLP-2R	301	310 CAGATTITTA GATCGCTCCT	320 TTCCTCATTC CAAGGAGACA	B30 GTCTTGTTAA ACTCAGAAGT	340 TATTATCAGT GCGCTAATTA	350 TGTGCATGTT TAAGGAGAAG
	Upstream	Initiator AT		J		_
			Do	wnstream Initi	iator ATG codoi	n.

Sequence alignment of the 5' end of the mGLP-2 receptor gene with the 5' end of the cDNA encoding the rat GLP-2R.

The 5' end of the cDNA encoding the rat GLP-2R (cloned by 5'-RACE) is presented in alignment with the corresponding region of sequence encoding the murine GLP-2R. The upstream initiator ATG codon is present in the rat sequence, and the downstream initiator ATG codon is conserved between in both the rat and murine sequences encoding the GLP-2R. The sequence corresponding to the putative 5'-UTR (untranslated region) is nearly identical between the rat and murine sequences presented.



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Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREO

Inventor(s): Daniel J. DRUCKER

Appl. No.: 09/833,740

FIG. 4

Hind III

Bam H1

Eco R1

Pvu II

PST I

Sal I

Xba I

Xho I

Hind III

Bam H1

Eco R1

Pvu II

PSTI

Sal I

Xba I

Xho I

4 KG

THE THE TEST

3.0

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREOF Inventor(s): Daniel J. DRUCKER

Appl. No.: 09/833,740

F16. 5

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREO Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

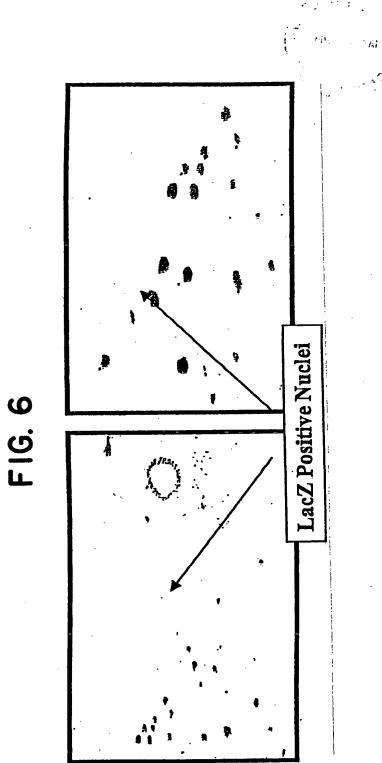
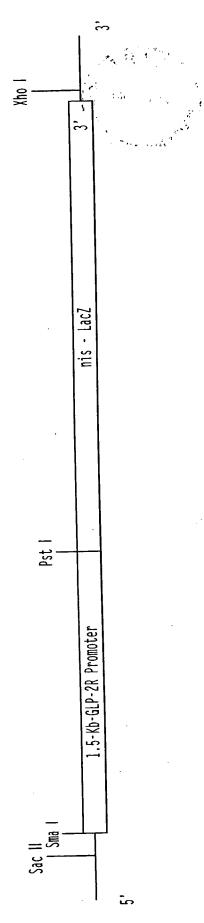


FIG. 78

aacacttcct ctctggacaa ggaggagtgc aggaggccac cgcctgcagt acatcttgga gtgttggagg gatgtgcctg cacttgtgaa cgggcgccag M R P Q P S P A V P S R C R E A P V P R V R A Q P V gaga ATG AGG CCC CAA CCA AGC CCG GCA GTG CCC AGT AGA TGC AGA GAG GCA CCC GTG CCC CGA GTG AGG GCA CAG CCA GTG G I P E A Q G P V P L H S Q M A GGC ATC CCT GAG GCC GAG GGG CCC GTT CCT CTC CAC TCC CAA CAG ATG 5'-UTR V. 5'-end rat GLP-2R cDNA rat GLP-2R cDNA rat GLP-2R cDNA

:1G. 7c

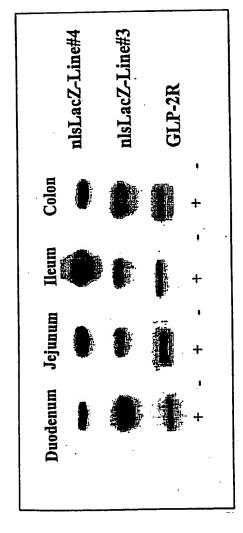


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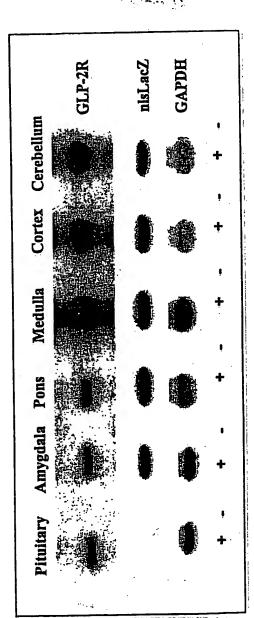
FIG. 7b

Anouse GLP-2R addictignt tittictictig ggictigated ggaaagtoccal ggaaagcacag ctgacttagg gglaagtotig ggaaaaatot human GLP-2R ccgccttigtt cittictcctc agcctggtdag ggaagtoccal ggaaagcacag ctgacttagg ga-aggictg ggaaagcacag ctgacttagg ga-aggictg ggaaagcacag ctgacttagg ga-aggictg ggaaagcacag ctgacttagg ga-aggictgag actctgaga actctgaag actctgaag actctgaag ttgctctaga mouse GLP-2R sccgccttgg gradaatett ggagggtgggggggggggggggggggggggggg
-203 -123 38 38 114 118 24
mouse GLP-2R human GLP-2R human GLP-2R mouse GLP-2R human GLP-2R human GLP-2R human GLP-2R mouse GLP-2R rat GLP-2R human GLP-2R mouse GLP-2R human GLP-2R

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREC Inventor(s): Daniel J. DRUCKE Appl. No.: 09/833,740



F16. 8a

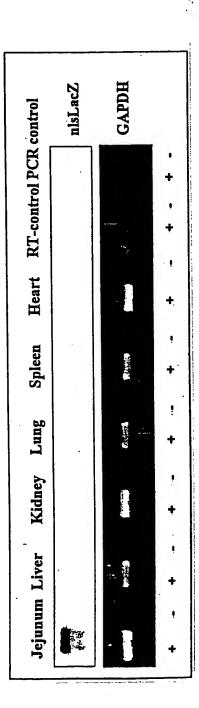


F1G. 8b

4

PROMOTER AND USES THEREOF Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

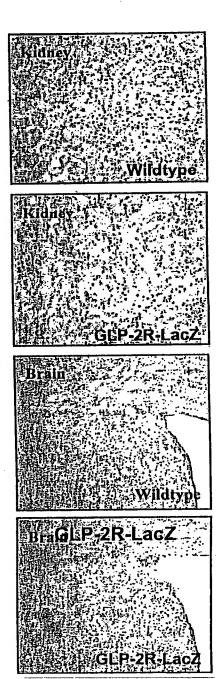
F16.8c



. .; ~• Title: GLP-2 RECEPTOR GENE
PROMOTER AND USES THEREO
Inventor(s): Daniel J. DRUCKER

Appl. No.: 09/833,740

FIG. 8d



Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREOF Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

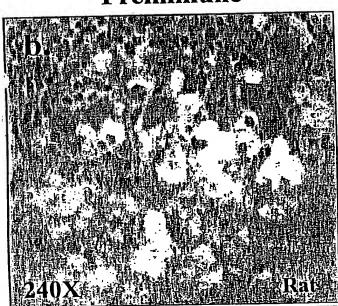
FIG. 9a

GLP-2R



FIG. 9b

Preimmune





Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THER Inventor(s): Daniel J. DRUCKEN. Appl. No.: 09/833,740

FIG. 9c



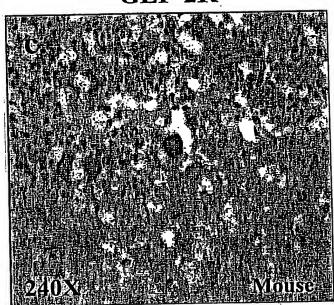
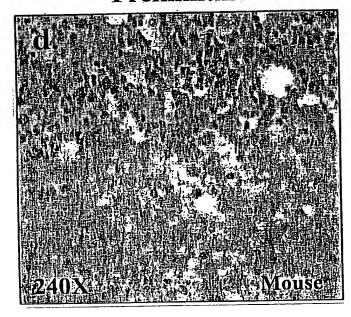
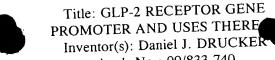


FIG. 9d

Preimmune





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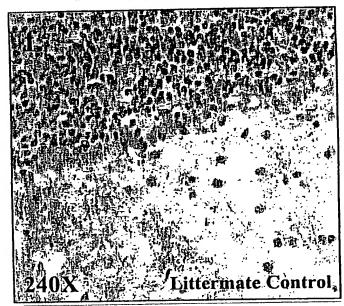
FIG. 9e

ß-Galactosidase



FIG. 9f

ß-Galactosidase





Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THERE Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740

GLP-2R

FIG. 10a

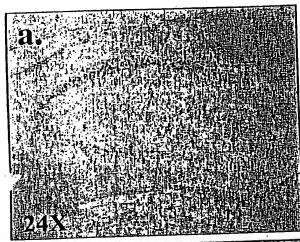


FIG. 10b

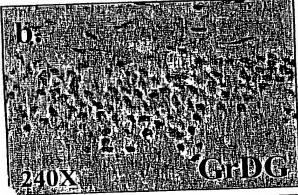
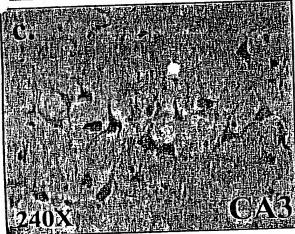


FIG. IOc



4



Title: GLP-2 RECEPTOR GENE
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Inventor(s): Daniel J. DRUCKER

Appl. No.: 09/833,740



β -Galactosidase

FIG. 10d

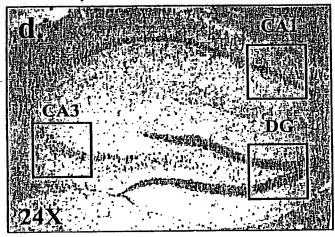


FIG. 10e

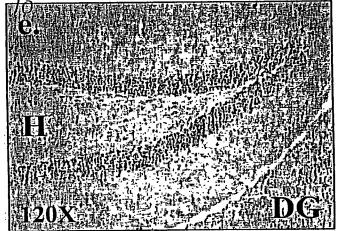
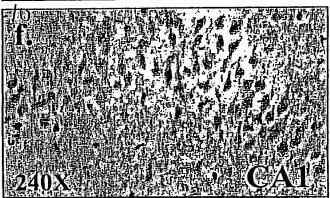


FIG. 10f



PROMOTER AND USES THEREO Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740





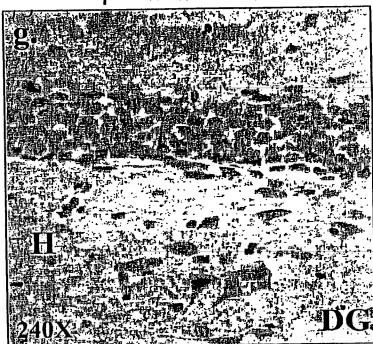
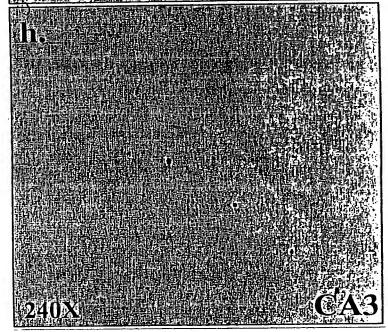


FIG. 10h



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FIG. Ila

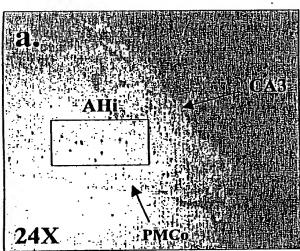


FIG. IIb

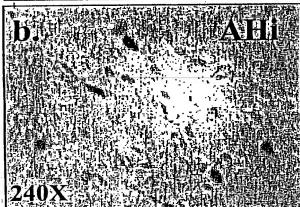
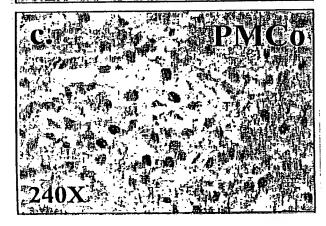


FIG. IIc



Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREO Inventor(s): Daniel J. DRUCKER Appl. No.: 09/833,740



FIG. IId

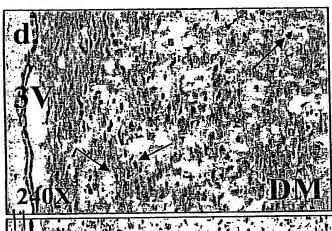


FIG. Ile

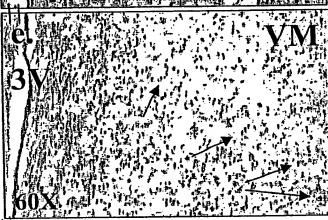
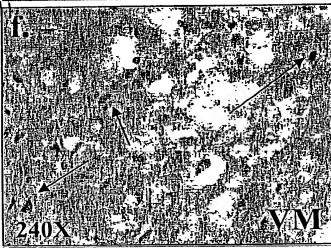


FIG. IIf





PROMOTER AND USES THERE Inventor(s): Daniel J. DRUCKEl Appl. No.: 09/833,740



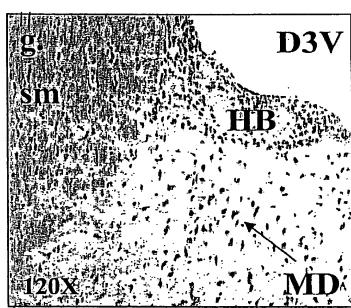
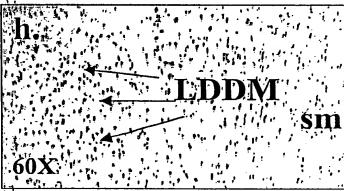


FIG. IIh



FIG, Ili

